

Exhibit A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Xiaofang WANG et al.

Application Number: 16/745,944

Confirmation Number: 8235

Filed: January 17, 2020

Art Unit: 1653

For: MESENCHYMAL-LIKE STEM CELLS
DERIVED FROM HUMAN EMBRYONIC
STEM CELLS, METHODS AND USES
THEREOF

Examiner: TBA

MS Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**RESPONSE TO NOTICE TO FILE MISSING PARTS OF APPLICATION &
PRELIMINARY AMENDMENT**

Dear Sir:

In response to the Notice to File Missing Parts of Nonprovisional Application dated February 7, 2020, Applicant respectfully submits the following fees due:

- \$75 application filing fee;
- \$330 search fee;
- \$380 examination fee;
- \$80 surcharge; and
- \$200 excess page fee.

Additionally, in advance of prosecution on the merits, please enter the following amendments:

Amendments to the Specification begin on page 3;

Amendments to the Drawings begin on page 4;

Amendments to the Claims begin on page 5; and

Applicant Remarks begin on page 6.

Finally, Applicant requests a Petition for a five-month Extension of Time and payment of the requisite fee accompanies this submission. Therefore, payment in the amount of \$2,565 (small entity status) covering the fees owed has been charged to our credit card. It is believed that all fees have now been paid; however, if the Patent Office believes that additional fees are due, then the Commissioner is hereby authorized to charge any other required fees, fees under § 1.17, or all required Extension of Time fees in any concurrently or future reply requiring a petition for an Extension of Time to Deposit Account No. 50-4570.

AMENDMENT TO THE SPECIFICATION

Please replace the Specification with the Substitute Specification attached hereto with markings showing changes in compliance with 37 C.F.R. § 1.125(b) and (c). A clean copy of the Specification is also attached. The Substitute Specification contains no new matter.

AMENDMENTS TO THE DRAWINGS

Applicant requests entry of the attached replacement sheets that include Figures 1A-1D, 2A-2C, 3A-3I, 4, 5A-5C, 8A-8B, 9A-9F, 13A-13D, 15A-15B, 16A-16B, 18A-18J, 21A-21D, 22A-22C, 23A-23B, 24A-24J, 28A-D, and 30. No new matter has been added.

AMENDMENT TO THE CLAIMS

Pursuant to 37 C.F.R. § 1.121 the following listing of claims will replace all prior versions and listings of claims in the application.

In the Claims:

1-92. (Cancelled)

93. (New) A method for producing embryoid bodies (EB) comprising:

- a. culturing human embryonic stem cells in a serum-free medium comprising at least one GSK3 inhibitor at a concentration ranging from 0.05 μM to 0.2 μM in the absence of feeder cells to form a human embryonic stem cell colony;
- b. dissociating the human embryonic stem cell colony in step a) to aggregates of human embryonic stem cells; and
- c. culturing the aggregates of human embryonic stem cells from step b) in an EB formation medium in an ultra-low-attachment dish to form embryonic bodies.

94. (New) A method for producing hemangioblast comprising:

- a. culturing human embryonic stem cells in a serum-free medium comprising at least one GSK3 inhibitor at a concentration ranging from 0.05 μM to 0.2 μM in the absence of feeder cells to form a human embryonic stem cell colony;
- b. dissociate the human embryonic stem cell colony in step a) to aggregates of human embryonic stem cells; and
- c. culturing the aggregates of human embryonic stem cells from step b) in an EB formation medium in an ultra-low-attachment dish to form embryonic bodies.
- d. disaggregating the EB resulting from step c) into single cells and culturing the single cells in a culture comprising at least one growth factor in an amount sufficient for the formation of human hemangio-colony forming cells.

95. (New) The method of claim 1, wherein the GSK3 inhibitor is (2'Z,3'E)-6-Bromoindirubin-3'-oxime (BIO).

96. (New) The method of claim 2, wherein the GSK3 inhibitor is (2'Z,3'E)-6-Bromoindirubin-3'-oxime (BIO).

REMARKS

Applicant respectfully requests that the Preliminary Amendment described herein be entered into the record prior to examination and consideration of the above-referenced application.

The Specification has been amended in accordance with 37 C.F.R. § 1.78 to claim the benefit of the earlier filing date and make a cross-reference to the related PCT application as well as to amend the Brief Description of the Drawings. No new matter has been added.

Applicant also submits herewith replacement sheets for Figures 1A-1D, 2A-2C, 3A-3I, 4, 5A-5C, 8A-8B, 9A-9F, 13A-13D, 15A-15B, 16A-16B, 18A-18J, 21A-21D, 22A-22C, 23A-23B, 24A-24J, 28A-D, and 30 in compliance with 37 C.F.R. §1.84 and 37 C.F.R. §1.121(d). No new matter has been added.

Claims 1-92 are cancelled. Claims 93-96 are new and particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. The new claims are fully supported by the originally filed claims and Specification. No new matter has been added.

Applicant respectfully requests prompt and favorable review of this application. If the undersigned can be of any assistance to the Examiner in addressing any issues that arise during examination of the present claims, then please contact Applicant's attorney at the number set forth below.

Respectfully submitted,

Dated: September 4, 2020

/susie s. cheng/
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Electronic Acknowledgement Receipt

EFS ID:	40475212
Application Number:	16745944
International Application Number:	
Confirmation Number:	8235
Title of Invention:	MESENCHYMAL-LIKE STEM CELLS DERIVED FROM HUMAN EMBRYONIC STEM CELLS, METHODS AND USES THEREOF
First Named Inventor/Applicant Name:	Xiaofang WANG
Customer Number:	76808
Filer:	Susie S. Cheng./Rebecca Wright
Filer Authorized By:	Susie S. Cheng.
Attorney Docket Number:	10143/003338-US3
Receipt Date:	04-SEP-2020
Filing Date:	17-JAN-2020
Time Stamp:	11:42:56
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$ 2565
RAM confirmation Number	E202094B43212555
Deposit Account	
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		02563091.PDF	143768	yes	10
			9421aeffe075754c739a4bbb7db14fe544d181df		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Applicant Arguments/Remarks Made in an Amendment		7	10	
	Claims		5	6	
	Drawings-only black and white line drawings		4	4	
	Specification		3	3	
	Applicant Response to Pre-Exam Formalities Notice		1	2	
Warnings:					
Information:					
2	Specification	02562807.PDF	900808	no	94
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Warnings:					
Information:					
3	Specification	02562808.PDF	899375	no	94
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Warnings:					
Information:					
4	Drawings-only black and white line drawings	02561579.PDF	1423345	no	20
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Warnings:					
Information:					

5	Fee Worksheet (SB06)	fee-info.pdf	<div>41188</div> <div>febac1d31b46817412ea976938f3b76f71f7e740</div>	no	2
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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.